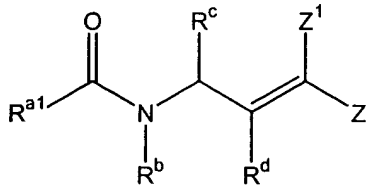
What is claimed is:

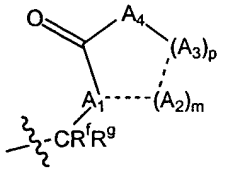
1. A compound of formula:



wherein:

R^{a1} is a cycloalkyl, heterocycloalkyl, aryl or heteroaryl group, provided that R^{a1} is not a substituted pyrrolidinyl, where the cycloalkyl, heterocycloalkyl, aryl or heteroaryl group is unsubstituted or substituted with one or more suitable substituents;

R^c is a substituent having the formula:



wherein:

R^f and R^g are each independently H or lower alkyl;

m is 0 or 1;

p is an integer of from 0 to 5;

A_1 is CH or N;

when p is 1, 2, 3, 4, or 5, A_2 is $C(R^h)(R^i)$, $N(R^j)$, S, S(O), $S(O)_2$, or O, and when p is 0, A_2 is $C(R^h)(R^i)(R^j)$, $N(R^i)(R^j)$, $S(R^i)$, $S(O)(R^i)$, $S(O)_2(R^i)$, or $O(R^i)$, where each R^h, R^i and R^j is independently H or a lower alkyl group;

each A_3 present is independently $C(R^h)(R^i)$, $N(R^j)$, S, S(O), $S(O)_2$, or O; where each R^h, R^i and R^j is independently H or lower alkyl;

when p is 1, 2, 3, 4, or 5, A_4 is $N(R^k)$, $C(R^h)(R^i)$, or O; and when p is 0, A_4 is $N(R^k)(R^l)$, $C(R^h)(R^i)(R^j)$, and $O(R^l)$, where each R^h, R^i and R^j is independently H or lower alkyl, each R^k is H, alkyl, aryl, or acyl, and each R^l is H, alkyl, or aryl;

provided that no more than two heteroatoms occur consecutively in the above-depicted ring formed by A_1, $(A_2)_m$, $(A_3)_p$, A_4, and C=O, where each dotted line in the ring depicts a single bond when A_2 is present and a hydrogen atom when A_2 is absent;

R^d is H, halogen, hydroxyl or an alkyl, alkoxy or alkylthio group, where the alkyl, alkoxy or alkylthio group is unsubstituted or substituted with one or more suitable substituents;

R^b is H or an alkyl group, unsubstituted or substituted with one or more suitable substituents;

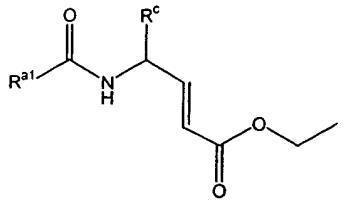
Z and Z^1 are each independently H, F, an alkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl group, where the alkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl group is unsubstituted or substituted with one or more suitable substituents, $-C(O)R^n$ $-CO_2R^n$ -CN, $-C(O)NR^nR^o$, $-C(O)NR^nOR^o$, $-C(S)R^n$, $-C(S)OR^n$ $-C(S)NR^nR^o$, $-C(=NR^n)R^o$, $-C(=NR^n)OR^o$, $-NO_2$, $-SOR^o$, $-SO_2R^n$, $-SO_2NR^nR^o$, $-SO_2(NR^n)(OR^o)$, $-SONR^n$, $-SO_3R^n$, $-PO(OR^n)_2$, $-PO(OR^n)(OR^o)$, $-PO(NR^nR^o)(OR^p)$, $-PO(NR^nR^o)(NR^pR^q)$, $-C(O)NR^nNR^oR^p$, $-C(S)NR^nNR^oR^p$, where R^n, R^o, R^p and R^q are each independently H or an alkyl, cycloalkyl, aryl, heterocycloalkyl, acyl or thioacyl group, where the alkyl, cycloalkyl, aryl, heterocycloalkyl, acyl or thioacyl group is unsubstituted or substituted with one or more suitable substituents, or where any two of the R^n, R^o, R^p and R^q, taken together with the atoms to which they are bonded, form a heterocycloalkyl group, which may be optionally substituted,

or Z and R^d, together with the atoms to which they are bonded, form a cycloalkyl or heterocycloalkyl group, where Z and R^d are as defined above except for moieties that cannot form the cycloalkyl or heterocycloalkyl group,

or Z and Z^1, together with the atoms to which they are bonded, form a cycloalkyl or heterocycloalkyl group, where Z and Z^1 are as defined above (except for moieties that cannot form the cycloalkyl or heterocycloalkyl group);

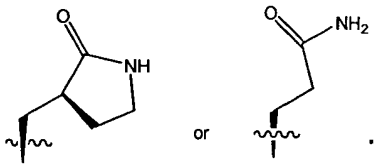
or a prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate thereof.

2. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claim 1 having the formula:



wherein R^{a1} is as defined in claim 1; and

R^c is

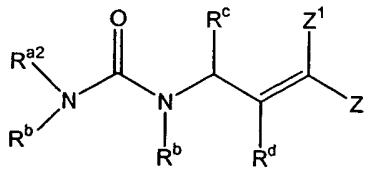


3. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claims 1 or 2, wherein R^{a1} is a $(C_3\text{-}C_8)$cycloalkyl, heterocycloalkyl, aryl or heteroaryl group, wherein the $(C_3\text{-}C_8)$cycloalkyl, heterocycloalkyl, aryl or heteroaryl group is unsubstituted or substituted with one or more substituents independently selected from $(C_1\text{-}C_4)$alkyl, aryl$(C_1\text{-}C_4)$alkyl, aryl, $(C_3\text{-}C_8)$cycloalkyl, heterocycloalkyl, heteroaryl, halo, hydroxyl, nitro, amino, $(C_1\text{-}C_4)$alkylamino, di-$(C_1\text{-}C_4)$alkylamino, aryl$(C_1\text{-}C_4)$alkoxy, aryloxy$(C_1\text{-}C_4)$alkyl, alkylenedioxy, aryloxy, $(C_3\text{-}C_8)$cycloalkoxy, heteroaryloxy, $(C_1\text{-}C_4)$haloalkyl, $(C_1\text{-}C_4)$alkoxy, $(C_1\text{-}C_4)$haloalkoxy, hydroxamino, $(C_1\text{-}C_4)$alkoxycarbonyl, $(C_1\text{-}C_4)$alkylcarbonylamino, $(C_1\text{-}C_4)$alkylcarbonyl, mercapto, alkylthio or arylthio, where the $(C_1\text{-}C_4)$alkyl and $(C_3\text{-}C_8)$cycloalkyl moieties thereof are optionally substituted by one or more of $(C_1\text{-}C_4)$alkyl (except for alkyl), halo, $(C_1\text{-}C_4)$haloalkyl, $(C_1\text{-}C_4)$alkoxy, $(C_1\text{-}C_4)$haloalkoxy and the heterocycloalkyl, aryl or heteroaryl moieties thereof are unsubstituted or are optionally substituted by one or more substituents independently selected from alkyl, haloalkyl, alkylenedioxy, nitro, amino, hydroxamino, alkylamino, dialkylamino, halo, hydroxyl, alkoxy, haloalkoxy, aryloxy, mercapto, alkylthio or arylthio groups.

4. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claims 1 or 2, wherein R^{a1} is a pyrazolyl, indolyl, chromenyl, benzofuranyl, benzothienyl, benzimidazolyl, triazolyl, quinolyl, thiazolidinyl, quinoxalinyl, phenyl or naphthyl group, where the pyrazolyl, indolyl, chromenyl, benzofuranyl, benzothienyl, benzimidazolyl, triazolyl, quinolyl, thiazolidinyl, quinoxalinyl, phenyl or naphthyl group is unsubstituted or substituted with one or more substituents independently selected from $(C_1\text{-}C_4)$alkyl, aryl$(C_1\text{-}C_4)$alkyl, aryl, halo, hydroxyl, nitro, amino, $(C_1\text{-}C_4)$alkylamino, di-$(C_1\text{-}C_4)$alkylamino, $(C_1\text{-}C_4)$alkoxy, aryl$(C_1\text{-}C_4)$alkoxy, aryloxy$(C_1\text{-}C_4)$alkyl, methylenedioxy, aryloxy, $(C_1\text{-}C_4)$haloalkyl, $(C_1\text{-}C_4)$haloalkoxy, $(C_1\text{-}C_4)$alkoxycarbonyl, $(C_1\text{-}C_4)$alkylcarbonylamino, or $(C_1\text{-}C_4)$alkylcarbonyl, where the $(C_1\text{-}C_4)$alkyl moieties thereof are optionally substituted by one or more of halo, $(C_1\text{-}C_4)$alkoxy or $(C_1\text{-}C_4)$haloalkoxy and the aryl moieties thereof are unsubstituted or are optionally substituted by one or more substituents independently selected from alkyl, haloalkyl, alkylenedioxy, nitro, amino, alkylamino, dialkylamino, halo, hydroxyl, alkoxy, haloalkoxy or aryloxy groups.

5. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claims 1 or 2, wherein R^{a1} is a is a pyrazolyl, indolyl, N-methylindolyl, chromenyl, benzofuranyl, benzothienyl, benzimidazolyl, , N-methylbenzimidazolyl, triazolyl, quinolyl, thiazolidinyl, quinoxalinyl, phenyl or naphthyl group, where the pyrazolyl, indolyl, chromenyl, benzofuranyl, benzothienyl, benzimidazolyl, triazolyl, quinolyl, thiazolidinyl, quinoxalinyl, phenyl or naphthyl group is unsubstituted or substituted with one or more substituents independently selected from methyl, ethyl, benzyl, phenethyl, phenyl, naphthyl, halo, hydroxyl, nitro, amino, methylamino, di-methylamino, methoxy, benzyloxy, methylenedioxy, $(C_1\text{-}C_4)$haloalkyl, $(C_1\text{-}C_4)$haloalkoxy, methoxycarbonyl, methylcarbonylamino, benzoyloxymethylene (phenylcarbonyloxymethyl-)or methylcarbonyl.

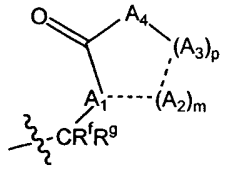
6. A compound of formula:



wherein:

R^{a2} is an alkyl, aryl or heteroaryl group, where the alkyl, aryl or heteroaryl group is unsubstituted or substituted with one or more suitable substituents; and

R^c is a substituent having the formula:



wherein:

R^f and R^g are each independently H or lower alkyl;

m is 0 or 1;

p is an integer of from 0 to 5;

A_1 is CH or N;

when p is 1, 2, 3, 4, or 5, A_2 is $C(R^h)(R^i)$, $N(R^j)$, S, S(O), $S(O)_2$, or O, and when p is 0, A_2 is $C(R^h)(R^i)(R^j)$, $N(R^i)(R^j)$, $S(R^i)$, $S(O)(R^i)$, $S(O)_2(R^i)$, or $O(R^i)$, where each R^h, R^i and R^j is independently H or a lower alkyl group;

each A_3 present is independently $C(R^h)(R^i)$, $N(R^j)$, S, S(O), $S(O)_2$, or O; where each R^h, R^i and R^j is independently H or lower alkyl;

when p is 1, 2, 3, 4, or 5, A_4 is $N(R^k)$, $C(R^h)(R^i)$, or O; and when p is 0, A_4 is $N(R^k)(R^l)$, $C(R^h)(R^i)(R^j)$, and $O(R^l)$, where each R^h, R^i and R^j is independently H or lower alkyl, each R^k is H, alkyl, aryl, or acyl, and each R^l is H, alkyl, or aryl;

provided that no more than two heteroatoms occur consecutively in the above-depicted ring formed by A_1, $(A_2)_m$, $(A_3)_p$, A_4, and C=O, where each dotted line in the ring depicts a single bond when A_2 is present and a hydrogen atom when A_2 is absent;

R^d is H, halogen, hydroxyl or an alkyl, alkoxy or alkylthio group, where the alkyl, alkoxy or alkylthio group is unsubstituted or substituted with one or more suitable substituents;

R^b is H or an alkyl group, unsubstituted or substituted with one or more suitable substituents;

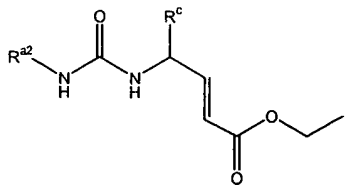
Z and Z^1 are each independently H, F, an alkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl group, where the alkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl group is unsubstituted or substituted with one or more suitable substituents, $-C(O)R^n$ $-CO_2R^n$ -CN, $-C(O)NR^nR^o$, $-C(O)NR^nOR^o$, $-C(S)R^n$, $-C(S)OR^n$ $-C(S)NR^nR^o$, $-C(=NR^n)R^o$, $-C(=NR^n)OR^o$, $-NO_2$, $-SOR^o$, $-SO_2R^n$, $-SO_2NR^nR^o$, $-SO_2(NR^n)(OR^o)$, $-SONR^n$, $-SO_3R^n$, $-PO(OR^n)_2$, $-PO(OR^n)(OR^o)$, $-PO(NR^nR^o)(OR^p)$, $-PO(NR^nR^o)(NR^pR^q)$, $-C(O)NR^nNR^oR^p$, $-C(S)NR^nNR^oR^p$, where R^n, R^o, R^p and R^q are each independently H or an alkyl, cycloalkyl, aryl, heterocycloalkyl, acyl or thioacyl group, where the alkyl, cycloalkyl, aryl, heterocycloalkyl, acyl or thioacyl group is unsubstituted or substituted with one or more suitable substituents, or where any two of the R^n, R^o, R^p and R^q, taken together with the atoms to which they are bonded, form a heterocycloalkyl group, which may be optionally substituted,

or Z and R^d, together with the atoms to which they are bonded, form a cycloalkyl or heterocycloalkyl group, where Z and R^d are as defined above except for moieties that cannot form the cycloalkyl or heterocycloalkyl group,

or Z and Z^1, together with the atoms to which they are bonded, form a cycloalkyl or heterocycloalkyl group, where Z and Z^1 are as defined above (except for moieties that cannot form the cycloalkyl or heterocycloalkyl group);

or a prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate thereof.

7. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claim 6, having the formula:



wherein:

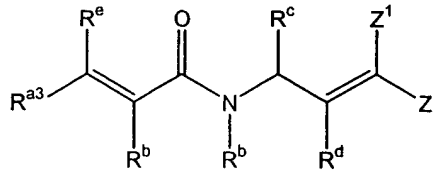
R^{a2} and R^c are as defined in claim 6.

8. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claims 6 or 7, wherein R^{a2} is a (C_1-C_4)alkyl, aryl or heteroaryl group, wherein the (C_1-C_4)alkyl, (C_3-C_8)cycloalkyl, heterocycloalkyl, aryl and heteroaryl group is unsubstituted or substituted with one or more suitable substituents.

9. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claims 6 or 7, wherein R^{a2} is a (C_1-C_4)alkyl, phenyl or naphthyl group, where the (C_1-C_4)alkyl group is unsubstituted or substituted with one or more substituents independently selected from halo, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_1-C_4 alkoxycarbonyl, and the phenyl or naphthyl group is unsubstituted or substituted with one or more substituents independently selected from halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, methylenedioxy and phenoxy.

10. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claims 6 or 7, wherein R^{a2} is a naphthyl, phenoxyphenyl, 3,5,-dimethoxyphenyl, 3,5-dimethylphenyl or an ethoxycarbonyl-substituted branched (C_1-C_6) alkyl moiety.

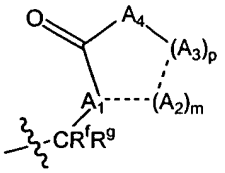
11. A compound of formula:



wherein:

R^{a3} is an aryl, heterocycloalkyl, heteroaryl or arylaminocarbonyl group, where the aryl, heterocycloalkyl, heteroaryl or arylaminocarbonyl group is unsubstituted or substituted with one or more suitable substituents; and

R^c is a substituent having the formula:



wherein:

R^f and R^g are each independently H or lower alkyl;

m is 0 or 1;

p is an integer of from 0 to 5;

A_1 is CH or N;

when p is 1, 2, 3, 4, or 5, A_2 is $C(R^h)(R^i)$, $N(R^j)$, S, S(O), $S(O)_2$, or O, and when p is 0, A_2 is $C(R^h)(R^i)(R^j)$, $N(R^i)(R^j)$, $S(R^i)$, $S(O)(R^i)$, $S(O)_2(R^i)$, or $O(R^i)$, where each R^h, R^i and R^j is independently H or a lower alkyl group;

each A_3 present is independently $C(R^h)(R^i)$, $N(R^j)$, S, S(O), $S(O)_2$, or O; where each R^h, R^i and R^j is independently H or lower alkyl;

when p is 1, 2, 3, 4, or 5, A_4 is $N(R^k)$, $C(R^h)(R^i)$, or O; and when p is 0, A_4 is $N(R^k)(R^l)$, $C(R^h)(R^i)(R^j)$, and $O(R^l)$, where each R^h, R^i and R^j is independently H or lower alkyl, each R^k is H, alkyl, aryl, or acyl, and each R^l is H, alkyl, or aryl;

provided that no more than two heteroatoms occur consecutively in the above-depicted ring formed by A_1, $(A_2)_m$, $(A_3)_p$, A_4, and C=O, where each dotted line in the ring depicts a single bond when A_2 is present and a hydrogen atom when A_2 is absent;

R^d is H, halogen, hydroxyl or an alkyl, alkoxy or alkylthio group, where the alkyl, alkoxy or alkylthio group is unsubstituted or substituted with one or more suitable substituents;

R^b is H or an alkyl group, unsubstituted or substituted with one or more suitable substituents;

R^e is H, halogen, hydroxyl or an alkyl, alkoxy or alkylthio group, where the alkyl, alkoxy or alkylthio group is unsubstituted or substituted with one or more suitable substituents;

Z and Z^1 are each independently H, F, an alkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl group, where the alkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl group is unsubstituted or substituted with one or more suitable substituents, $-C(O)R^n$

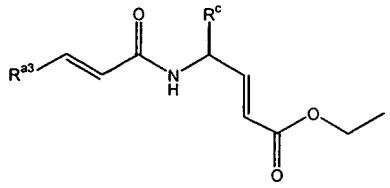
$-CO_2R^n$ -CN, $-C(O)NR^nR^o$, $-C(O)NR^nOR^o$, $-C(S)R^n$, $-C(S)OR^n$ $-C(S)NR^nR^o$, $-C(=NR^n)R^o$, $-C(=NR^n)OR^o$, $-NO_2$, $-SOR^o$, $-SO_2R^n$, $-SO_2NR^nR^o$, $-SO_2(NR^n)(OR^o)$, $-SONR^n$, $-SO_3R^n$, $-PO(OR^n)_2$, $-PO(OR^n)(OR^o)$, $-PO(NR^nR^o)(OR^p)$, $-PO(NR^nR^o)(NR^pR^q)$, $-C(O)NR^nNR^oR^p$, $-C(S)NR^nNR^oR^p$, where R^n, R^o, R^p and R^q are each independently H or an alkyl, cycloalkyl, aryl, heterocycloalkyl, acyl or thioacyl group, where the alkyl, cycloalkyl, aryl, heterocycloalkyl, acyl or thioacyl group is unsubstituted or substituted with one or more suitable substituents, or where any two of the R^n, R^o, R^p and R^q, taken together with the atoms to which they are bonded, form a heterocycloalkyl group, which may be optionally substituted,

or Z and R^d, together with the atoms to which they are bonded, form a cycloalkyl or heterocycloalkyl group, where Z and R^d are as defined above except for moieties that cannot form the cycloalkyl or heterocycloalkyl group,

or Z and Z^1, together with the atoms to which they are bonded, form a cycloalkyl or heterocycloalkyl group, where Z and Z^1 are as defined above (except for moieties that cannot form the cycloalkyl or heterocycloalkyl group);

or a prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate thereof.

12. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claim 11, having the formula:



wherein:

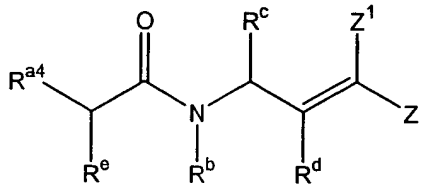
R^{a3} and R^c are as defined in claim 11.

13. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claims 11 or 12, wherein R^{a3} is a aryl, heterocycloalkyl, heteroaryl or arylaminocarbonyl group, wherein the aryl, heterocycloalkyl, heteroaryl or arylaminocarbonyl group is unsubstituted or substituted with one or more substituents independently selected from (C_1-C_4)alkyl, aryl, halo, hydroxyl, nitro, amino, di-(C_1-C_4)alkylamino (C_1-C_4)alkoxy, alkylenedioxy, aryloxy, where the (C_1-C_4)alkyl or aryl moieties thereof are unsubstituted or optionally substituted by one or more of (C_1-C_4)alkyl (except for alkyl), halo, (C_1-C_4)haloalkyl, (C_1-C_4)alkoxy, (C_1-C_4)haloalkoxy, alkylenedioxy groups.

14. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claims 11 or 12, wherein R^{a3} is a phenyl or phenylaminocarbonyl group, where the phenyl group or phenyl moiety of the phenylaminocarbonyl group is unsubstituted or substituted with one or more substituents independently selected from (C_1-C_4)alkyl, halo, hydroxyl, nitro, (C_1-C_4)alkoxy and alkylenedioxy.

15. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claims 11 or 12, wherein R^{a3} is a phenyl or phenylaminocarbonyl group, where the phenyl group or phenyl moiety of the phenylaminocarbonyl group is unsubstituted or substituted with one or more substituents independently selected from methyl, halo, hydroxyl, nitro, methoxy, and alkylenedioxy.

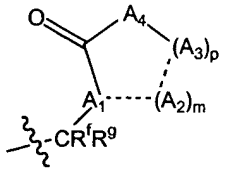
16. A compound of formula:



wherein:

R^{a4} is an aryloxy, heteroaryloxy, alkyloxy, cycloalkyloxy, heterocycloalkyloxy, aryl, cycloalkyl, or heteroaryl group, where the aryloxy, heteroaryloxy, alkyloxy, cycloalkyloxy, heterocycloalkyloxy, aryl, cycloalkyl, or heteroaryl group is unsubstituted or substituted with one or more suitable substituents; and

R^c is a substituent having the formula:



wherein:

R^f and R^g are each independently H or lower alkyl;

m is 0 or 1;

p is an integer of from 0 to 5;

A_1 is CH or N;

when p is 1, 2, 3, 4, or 5, A_2 is $C(R^h)(R^i)$, $N(R^j)$, S, S(O), $S(O)_2$, or O, and when p is 0, A_2 is $C(R^h)(R^i)(R^j)$, $N(R^i)(R^j)$, $S(R^i)$, $S(O)(R^i)$, $S(O)_2(R^i)$, or $O(R^i)$, where each R^h, R^i and R^j is independently H or a lower alkyl group;

each A_3 present is independently $C(R^h)(R^i)$, $N(R^j)$, S, S(O), $S(O)_2$, or O; where each R^h, R^i and R^j is independently H or lower alkyl;

when p is 1, 2, 3, 4, or 5, A_4 is $N(R^k)$, $C(R^h)(R^i)$, or O; and when p is 0, A_4 is $N(R^k)(R^l)$, $C(R^h)(R^i)(R^j)$, and $O(R^l)$, where each R^h, R^i and R^j is independently H or lower alkyl, each R^k is H, alkyl, aryl, or acyl, and each R^l is H, alkyl, or aryl;

provided that no more than two heteroatoms occur consecutively in the above-depicted ring formed by A_1, $(A_2)_m$, $(A_3)_p$, A_4, and C=O, where each dotted line in the ring depicts a single bond when A_2 is present and a hydrogen atom when A_2 is absent;

R^d is H, halogen, hydroxyl or an alkyl, alkoxy or alkylthio group, where the alkyl, alkoxy or alkylthio group is unsubstituted or substituted with one or more suitable substituents;

R^b is H or an alkyl group, unsubstituted or substituted with one or more suitable substituents;

R^e is H, halogen, hydroxyl or an alkyl, alkoxy or alkylthio group, where the alkyl, alkoxy or alkylthio group is unsubstituted or substituted with one or more suitable substituents;

Z and Z^1 are each independently H, F, an alkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl group, where the alkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl group is unsubstituted or substituted with one or more suitable substituents, $-C(O)R^n$ $-CO_2R^n$ -CN, $-C(O)NR^nR^o$, $-C(O)NR^nOR^o$, $-C(S)R^n$, $-C(S)OR^n$ $-C(S)NR^nR^o$, $-C(=NR^n)R^o$, $-C(=NR^n)OR^o$, $-NO_2$, $-SOR^o$, $-SO_2R^n$, $-SO_2NR^nR^o$, $-SO_2(NR^n)(OR^o)$, $-SONR^n$, $-SO_3R^n$, $-PO(OR^n)_2$, $-PO(OR^n)(OR^o)$, $-PO(NR^nR^o)(OR^p)$, $-PO(NR^nR^o)(NR^pR^q)$, $-C(O)NR^nNR^oR^p$, $-C(S)NR^nNR^oR^p$, where R^n, R^o, R^p and R^q are each independently H or an alkyl, cycloalkyl, aryl, heterocycloalkyl, acyl or thioacyl group, where the alkyl, cycloalkyl, aryl, heterocycloalkyl, acyl or thioacyl group is unsubstituted or substituted with one or more suitable substituents, or where any two of the R^n, R^o, R^p and R^q, taken together with the atoms to which they are bonded, form a heterocycloalkyl group, which may be optionally substituted,

or Z and R^d, together with the atoms to which they are bonded, form a cycloalkyl or heterocycloalkyl group, where Z and R^d are as defined above except for moieties that cannot form the cycloalkyl or heterocycloalkyl group,

or Z and Z^1, together with the atoms to which they are bonded, form a cycloalkyl or heterocycloalkyl group, where Z and Z^1 are as defined above (except for moieties that cannot form the cycloalkyl or heterocycloalkyl group);

or a prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate thereof.

17. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claim 16, wherein R^{a4} is an aryloxy, heteroaryloxy, (C_1-C_4)alkoxy, (C_3-C_8)cycloalkoxy, heterocycloalkyloxy, (C_3-C_8)cycloalkyl, heteroaryl or (C_1-C_4)alkoxycarbonyl group, wherein the aryloxy, heteroaryloxy, (C_1-C_4)alkoxy, (C_3-C_8)cycloalkoxy, heterocycloalkyloxy, (C_3-C_8)cycloalkyl, heteroaryl or (C_1-C_4)alkoxycarbonyl group is unsubstituted or substituted with one or more substituents independently selected from (C_1-C_4)alkyl, aryl, (C_3-C_8)cycloalkyl, heterocycloalkyl, heteroaryl, halo, hydroxyl, (C_1-C_4)alkoxy, alkylenedioxy, aryloxy, (C_3-C_8)cycloalkoxy, heteroaryloxy and (C_1-C_4)alkoxycarbonyl, where the (C_1-C_4)alkyl, aryl, (C_3-C_8)cycloalkyl, heterocycloalkyl, heteroaryl moieties thereof are optionally substituted by one or more of (C_1-C_4)alkyl (except for alkyl), halo, (C_1-C_4)haloalkyl, (C_1-C_4)alkoxy, (C_1-C_4)haloalkoxy, alkylenedioxy, aryl or heteroaryl, where the aryl or heteroaryl is unsubstituted or substituted with one or more substituents independently selected from alkyl, haloalkyl, alkylenedioxy, nitro, amino, hydroxamino, alkylamino, dialkylamino, halo, hydroxyl, alkoxy, haloalkoxy, aryloxy, mercapto, alkylthio or arylthio groups.

18. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to claim 16, wherein R^{a4} is a phenoxy, or (C_1-C_4)alkoxycarbonyl group, wherein the phenyl moiety of the phenoxy group is unsubstituted or substituted with one or more substituents independently selected from halo and (C_1-C_4)alkoxy.

19. A compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate according to any one of claims 1, 6, 11 or 16, wherein:

A_1 is CH or N;

A_2 is $C(R^h)(R^i)$, $N(R^j)$, S, S(O), $S(O)_2$, or O; where each R^h, R^i and R^j is independently H or lower alkyl;

each A_3 present is independently $C(R^h)(R^i)$, $N(R^j)$, S, S(O), $S(O)_2$, or O; where each R^h, R^i and R^j is independently H or lower alkyl;

when p is 1, 2, 3, 4, or 5, A_4 is $N(R^k)$, $C(R^h)(R^i)$, or O; and when p is 0, A_4 is $N(R^k)(R^l)$, $C(R^h)(R^i)(R^j)$, and $O(R^l)$, where each R^h, R^i and R^j is independently H or

lower alkyl, each R^k is H, alkyl, aryl, or acyl, and each R^l is H, alkyl, or aryl; provided that no more than two heteroatoms occur consecutively in the above-depicted ring formed by A_1, $(A_2)_m$, $(A_3)_p$, A_4, and C=O, where each dotted line in the ring depicts a single bond when A_2 is present and a hydrogen atom when A_2 is absent;

Z and Z^1 are independently H, F, a unsubstituted or substituted alkyl group, cycloalkyl group, heterocycloalkyl group, aryl group or heteroaryl group, $-C(O)R^n$, $-CO_2R^n$, -CN, $-C(O)NR^nR^o$, $-C(O)NR^nOR^o$, $-C(S)R^n$, $-C(S)NR^nR^o$, $-NO_2$, $-SOR^o$, $-SO_2R^n$, $-SO_2NR^nR^o$, $-SO_2(NR^n)(OR^o)$, $-SONR^n$, $-SO_3R^n$, $-PO(OR^n)_2$, $-PO(OR^n)(OR^o)$, $-PO(NR^nR^o)(OR^p)$, $-PO(NR^nR^o)(NR^pR^q)$, $-C(O)NR^nNR^oR^p$, $-C(S)NR^nNR^oR^p$, where each R^n, R^o, R^p and R^q are independently H or an alkyl, cycloalkyl, aryl, heterocycloalkyl, acyl or thioacyl group, where the alkyl, cycloalkyl, aryl, heterocycloalkyl, acyl or thioacyl group is unsubstituted or substituted with one or more suitable substituents, or where any two of the R^n, R^o, R^p and R^q, taken together with the atoms to which they are bonded, form a heterocycloalkyl group, which may be optionally substituted, form a heterocycloalkyl group, provided that Z and Z^1 are not both H;

or Z and R^d, together with the atoms to which they are bonded, form a cycloalkyl or heterocycloalkyl group, where Z and R^d are as defined above except for moieties that cannot form the cycloalkyl or heterocycloalkyl group;

or Z and Z^1, together with the atoms to which they are bonded, form a cycloalkyl or heterocycloalkyl group, where Z and Z^1 are as defined above except for moieties that cannot form the cycloalkyl or heterocycloalkyl group.

20. The compound according to claims 1, 6, 11 or 16, having antipicornaviral activity corresponding to an EC_{50} less than or equal to 100 μM in an H1-HeLa cell culture assay.

21. A pharmaceutical composition comprising:

a therapeutically effective amount of at least one antipicornaviral agent selected from compounds, prodrugs, pharmaceutically acceptable salts, pharmaceutically active metabolites, and pharmaceutically acceptable solvates defined in claims 1, 6, 11 or 16; and

a pharmaceutically acceptable carrier, diluent, vehicle, or excipient.

22. A method of treating a mammalian disease condition mediated by picornaviral protease activity, comprising administering to a mammal in need thereof a therapeutically effective amount of at least one compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate defined in claims 1, 6, 11 or 16.

23. A method of inhibiting the activity of a picornaviral 3C protease, comprising contacting the picornaviral 3C protease with an effective amount of at least one compound, prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate defined in claims 1, 6, 11 or 16,.

24. The method as defined in claim 23, wherein the picornaviral 3C protease is a rhinoviral protease.

25. A compound selected from the group:

4*S*-[(naphthalene-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(naphthalene-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3-*R*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[3-(3-bromo-phenyl)-acryloylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

N-[3-ethoxycarbonyl-1*S*-(2-oxo-pyrrolidin-3*R*-ylmethyl)-ally]-terephthalamic acid methyl ester;

4*S*-[3-(3,4-dimethoxy-phenyl)-acryloylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(5-bromo-pyridine-3-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(3-hydroxyquinoxaline-2-carbonyl)-amino]-5-(2-oxopyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(5-ethyl-1H-indole-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-(3-benzo[1,3]dioxol-5-yl-acryloylamino)-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4-[(1H-benzoimidazole-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[3-(4-chloro-phenyl)-acryloylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

5-(2-oxo-pyrrolidin-3*S*-yl)-4*S*-(3-p-tolyl-acryloylamino)-pent-2-enoic acid ethyl ester;

4*S*-[(3-acetyl-2-phenyl-thiazolidine-4-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(5-bromo-benzofuran-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[3-(4-nitro-phenyl)-acryloylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[3-(methoxy-phenyl)-acryloylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[3-(3-hydroxy-phenyl)-acryloylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(6,7-dimethoxy-naphthalene-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(5,6-dimethoxy-1-methyl-indole-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(5-bromo-1H-indole-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid;

4*S*-[(5-bromo-1-methyl-indole-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(3-acetylamino-naphthalene-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*[3-(3-bromo-4-methyl-phenyl)-acryloylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[3-(1*S*-ethoxycarbonyl-3-methyl-butyl)-ureido]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

6-carbamoyl-4*S*-[(naphthalene-2-carbonyl)-amino]-hex-2-enoic acid ethyl ester;

4*S*-[(benzo[b]thiophene-2-carbonyl)-amino]-6-carbamoyl-hex-2-enoic acid ethyl ester;

6-carbamoyl-4*S*-(4-dimethylamino-benzylamino)-hex-2-enoic acid ethyl ester;

6-carbamoyl-4*S*-[(quinoxaline-2-carboxyl)-amino]-hex-2-enoic acid ethyl ester;

6-carbamoyl-4*S*-(3-phenyl-acryloylamino)-hex-2-enoic acid ethyl ester;

4*S*-[3-(3-bromophenyl)-acryloylamino]-6-carbamoyl-hex-2-enoic acid ethyl ester;

6-carbamoyl-4*S*-[(quinoline-2-carbonyl)-amino]-hex-2-enoic acid ethyl ester;

6-carbamoyl-4*S*-[(5-methyl-2-phenyl-2H-[1,2,3] triazole-4-carbonyl)-amino]-hex-2-enoic acid ethyl ester;

4*S*-[(2-benzyl-5-tert-butyl-2H-pyrazole-3-carbonyl)-amino]-6-carbamoyl-hex-2-enoic acid ethyl ester;

4*S*-benzylamino-6-carbamoyl-hex-2-enoic acid ethyl ester;

6-carbamoyl-4*S*-(3,4-dichloro-benzoylamino)-hex-2-enoic acid ethyl ester;

benzoic acid-2-[1*S*-2-carbamoyl-ethyl)-3-ethoxycarbonyl-allylcarbamoyl]-benzyl ester;

6-carbamoyl-4*S*-(2-phenethyl-benzoylamino)--hex-2-enoic acid ethyl ester;

6-carbamyl-4*S*-[(1H-indole-2-carbonyl)-amino]-hex-2-enoic acid ethyl ester;

4*S*-[(5-fluoro-1H-indole-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(5-chloro-1H-indole-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(5-methoxy-1H-indole-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(7-nitro-1H-indole-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4-[(5-methyl-1H-indole-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(6-chloro-2H-chromene-3-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(2-methyl-5-phenyl-furan-3-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(6-benzyloxy-5-methoxy-1H-indole-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(1H-indole-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[3-(3-bromo-4-fluoro-phenyl)-acryloylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[3-(6-bromo-benzo[1,3]dioxol-5-yl)-acryloylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

5-(2-oxo-pyrrolidin-3*S*-yl)-4*S*-[3-(2,4,6-trimethyl-phenylcarbamoyl)-acryloylamino]-pent-2-enoic acid ethyl ester;

4*S*-[(6-methyl-naphthalene-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(6-bromo-*2H*-chromene-3-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(7-bromo-naphthalene-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[(7-hydroxy-naphthalene-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

5-(2-oxo-pyrrolidin-3*S*-yl)-4*S*-[3-(2-phenoxy-phenyl)-ureido]-pent-2-enoic acid ethyl ester;

4*S*-(3-naphthalen-1-yl)-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[3-(3,5-dimethoxy-phenyl)ureido]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[3-(3,5-dimethyl-phenyl)-ureido]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

6-carbamoyl-4S-[3-(1-ethoxycarbonyl-3-methylbutyl)-ureido]-hex-2-enoic acid ethyl ester;

4*S*-[2-(3-methoxy-phenoxy)-acetylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[2-(3-chloro-phenoxy)-acetylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[2-(3,4-dichloro-phenoxy)-acetylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4*S*-[2-(3-chloro-phenyl)-acetylamino]-5-(2-oxo-pyrrolidin-3*S*-yl)-pent-2-enoic acid ethyl ester;

4S-[3-(2,5-dibromo-phenyl)-acryloylamino]-5-(2-oxo-pyrrolidin-3S-yl)-pent-2-enoic acid ethyl ester;

4S-[(6-hydroxy-naphthalene-2-carbonyl)-amino]-5-(2-oxo-pyrrolidin-3S-yl)-pent-2-enoic acid ethyl ester;

4S-[(6-bromo-7-methyl-2H-chromene-3-carbonyl) amino]-5-(2-oxo-pyrrolidin-3S-yl)-pent-2-enoic acid ethyl ester;

4S-[(2H-chromene-3-carbonyl)- amino]-5-2-oxopyrrolidin-3S-yl)-pent-2-enoic acid ethyl ester;

4S-[(4-bromo-6-methyl-naphthalene-2-carbonyl) amino]-5-(2-oxo-pyrrolidin-3S-yl)-pent-2-enoic acid ethyl ester;

4S-[(3-amino-naphthalene-2-carbonyl)- amino]-5-(2-oxo-pyrrolidin-3S-yl)-pent-2-enoic acid ethyl ester;

and or a prodrug, pharmaceutically acceptable salt, pharmaceutically active metabolite, or pharmaceutically acceptable solvate thereof.